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CASE REPORTS

Reversal of Chronic Regional Myocardial Dysfunction (Hibernating Myocardium) by Synchronized Diastolic Coronary Venous Retroperfusion During Coronary Angioplasty

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A 62 year old man with previous myocardial infarction, an occluded right coronary artery and a 90% stenosis of the left anterior descending coronary artery underwent angioplasty with the support of coronary venous retroperfusion of arterial blood during the procedure. In two of four angioplasty balloon dilations of the left anterior descending coronary artery, synchronized diastolic retroperfusion of the coronary veins with arterial blood was applied to protect the severely dysfunctioning myocardium from additional ischemia. Two-dimensional echocardiography was used to monitor and quantitate alterations in left ventricular function.

Retroperfusion of arterial blood resulted in immediate improvement in ischemic zone wall motion despite the totally occluded artery during balloon dilation. Echocardiographic images recorded after angioplasty showed a marked improvement in contraction of the previously dyskinetic segments, with changes similar to those seen during balloon dilations with synchronized diastolic coronary venous retroperfusion. Thus, in this patient, viability of chronically dysfunctioning myocardium could be demonstrated by the improvement in regional wall motion during retroperfusion.

This technique could eventually be of value to elucidate the anatomic location of viable myocardium while maintaining adequate left ventricular systolic function during coronary artery interventions in the catheterization laboratory.

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With growing experience in myocardial revascularization, it has been realized that many of these interventions may restore myocardial contraction in patients with chronically impaired left ventricular function (1–4) demonstrating viable but hibernating myocardium. Synchronized retroperfusion of arterial blood through the coronary veins for treatment of acutely ischemic myocardium has been extensively investigated in experimental animals (5–7). Recent studies (8,9) have also demonstrated that retroperfusion can improve ischemic myocardial dysfunction in different clinical situations. We recently witnessed that retroperfusion may improve function of chronically ischemic and dyssynergic areas of the left ventricle during angioplasty balloon dilation of the left anterior descending coronary artery. Thus, it is possible that such contractile responses could predict the presence of viable myocardium while protecting against ischemia during angioplasty balloon inflations.

Methods

The synchronized retroperfusion system. This system (Retroperfusion Systems, Inc.) consists of an electronic pumping console, an arterial catheter and the retroperfusion catheter. It is designed to provide the patient's own oxygenated blood to the ischemic myocardium through the coronary veins. Arterial blood is shunted from the patient's femoral artery with the use of an 8F catheter connected to the inlet of the pumping cassette. The disposable pumping cassette is aligned within the electronic housing of the console. Arterial blood is pumped during diastole by a piston

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that is activated by electrocardiographic (ECG) triggering. The outlet of the pumping cassette is connected to the retroperfusion catheter, which is a radiopaque, triple lumen, 8.5F catheter with a gas-inflated balloon located 1 cm from the distal end. The gas inflation lumen inflates the balloon (10 mm in diameter at full pressure) during diastole with a fixed volume of gas (carbon dioxide) from a pressurized cylinder in synchronization with each pump stroke. The pressure lumen is used to monitor coronary venous pressure before and during retroperfusion. The third lumen is the infusion lumen, which is connected to the outlet tubing of the pumping cassette. The retroperfusion catheter is introduced into the coronary sinus through the jugular vein and, in this manner, arterial blood is propelled forward during diastole into the coronary venous system, while flow is stopped during systole to allow for coronary venous drainage. The system can operate with flow rates of up to 250 ml/min.

Two-dimensional echocardiography. During the angioplasty procedure, left ventricular wall motion was monitored by two-dimensional echocardiography. Apical two and four chamber view recordings obtained before and after angioplasty and four chamber view images before and at the end of balloon inflations were subsequently digitized from videotape into a cine loop format by using a commercial computerized analysis system (MicroSonics, Inc.). Images were selected at equal time points during the nonretroperfused and retroperfused balloon inflations. The centerline method, as described by Sheehan et al. (10) and implemented in our laboratory, was used to quantify left ventricular wall motion imaged by two-dimensional echocardiography. Chord shortening factors of different left ventricular regions were averaged, and changes in the same regions from before to after angioplasty, as well as changes from baseline to peak balloon inflations, were quantitatively presented.

Case Report

Clinical features. The patient is a 62 year old white man with a history of an inferior myocardial infarction 15 years previously. He has been asymptomatic since then. Five months before the present hospital admission, he experienced retrosternal pain associated with diaphoresis during a 30 min period. Two days later, the ECG revealed T wave inversions in leads I, aVL and V_2 to V_6. Two months later, he was admitted to the hospital because of progressively increasing angina and exertional dyspnea. At that time, there were persistent Q waves in leads V_1 to V_3, indicating an old anteroseptal myocardial infarction and ST-T wave abnormalities suggesting lateral ischemia. As a remnant of the first inferior infarction, there were persistent Q waves in leads II and III (Fig. 1).

Cardiac catheterization. Coronary angiography revealed the right coronary artery to be totally occluded and supplied by collateral vessels from the left anterior descending coronary artery, which had a 90% proximal stenosis. The right anterior oblique ventriculogram showed severe hypokinesia in the inferior, apical, septal and anterolateral walls. Left ventricular ejection fraction was 35%.

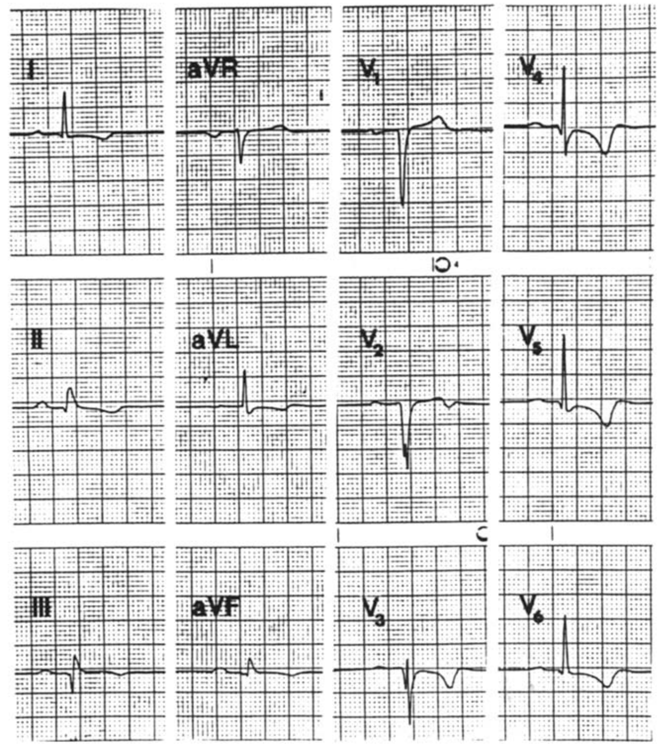

Figure 1. Twelve lead electrocardiogram recorded before the angioplasty procedure, showing previous inferior and anteroseptal myocardial infarction and diffuse T wave changes.

Therapeutic implications. The patient rejected coronary bypass surgery and requested an angioplasty procedure. The cardiologist considered the patient at high risk for angioplasty because of the decreased global left ventricular function, the occluded right coronary artery and the severe stenosis of the left anterior descending coronary artery with left to right collateral flow. He requested synchronized coronary venous retroperfusion to support myocardial function during angioplasty of the left anterior descending artery lesion. This is an ongoing protocol of retroperfusion support during high risk angioplasty in our institution.

Coronary angioplasty and coronary venous retroperfusion. After the patient gave informed written consent, angioplasty was performed through the right femoral artery. The retroperfusion catheter was placed in the distal great cardiac vein through the right internal jugular vein, and coronary venous pressure was monitored throughout the procedure. The patient received 15,000 U of intravenous heparin during a 1 h period, with an activated clotting time maintained close to 250 s. No other cardiac medication was given during the procedure. The angioplasty balloon was inflated on four occasions for a duration of 120, 90, 80 and 90 s, respectively. The second and fourth balloon inflations were undertaken during retroperfusion. Mean aortic pressure (between 100 and 120 mm Hg) and heart rate (between 60 and 72 beats/min) were not significantly altered during the angioplasty balloon inflations irrespective of the application of retroperfusion. The retrograde blood flow delivered by the pump system into the coronary veins was 125 ml/min during the two balloon inflations supported by retroperfusion. Coronary sinus pressure was 5 versus 11 mm Hg during the first and third balloon inflations (without retroperfusion) and was 20 versus 19 mm Hg during the second and fourth inflations (with retroperfusion). The first and third balloon inflations (without retroperfusion) had to be stopped because of severe oppressive chest pain. Only slight chest discomfort was reported by the patient during the second balloon inflation, and no pain was experienced during the fourth inflation.

Echocardiographic findings. Before angioplasty, two-dimensional echocardiography revealed wall motion abnormalities in locations similar to those noted on the left ventriculogram. Two areas of dyskinesia, one apical (Fig. 2A, chords 40 to 59) and one in the distal inferior wall (Fig. 2C, chords 18 to 37) were noted. Balloon inflations while the myocardium was not protected by retroperfusion resulted in decreased contraction of the proximal septum (Fig. 2B, chords 5 to 26) as compared with baseline. When retroperfusion was applied during angioplasty balloon inflation, contraction of the septal and apical regions improved (Fig. 2B, chords 5 to 26 and 27 to 43) compared with baseline and balloon inflation without retroperfusion.

After successful dilation of the left anterior descending coronary artery, the dysfunctioning regions supplied by that artery became synergic as measured in the four chamber view (Fig. 2A), with an average improvement in chord shortening from −0.85 to 1.18 in the apical area (chords 40 to 59) and from 1.53 to 2.47 in the septum (chords 17 to 39). This improvement in wall motion after the angioplasty was very similar to that seen during the balloon dilations supported with retroperfusion (Fig. 2A and B). Contraction in the posteroinferior wall and the anteroapical regions also improved (Fig. 2C).

Discussion

In the present case, successful percutaneous transluminal coronary angioplasty reopened the left anterior descending coronary artery, resulting in immediate improvement in the widespread chronic regional left ventricular contraction abnormalities despite two previous myocardial infarctions. The institution of synchronized diastolic coronary venous retroperfusion improved contraction of the left ventricle during balloon occlusion of the left anterior descending coronary artery. The improved contraction pattern during angioplasty balloon inflations combined with retroperfusion was very similar to that noted in the final outcome after successful angioplasty. Synchronized diastolic coronary venous retroperfusion thereby predicted viability of previously compromised areas of the myocardium. The effective dilation of the tight left anterior descending artery stenosis resulted in improved contraction of the septum and apex despite ECG signs of a previous "transmural" infarction in this region. The improvement in the inferior wall contraction abnormality after successful balloon dilation of the left anterior descending artery was probably due to increased collateral circulation to the territory of the totally occluded right coronary artery.

Viability of chronically dysfunctioning myocardium. The possibility of improving chronically impaired left ventricular function with revascularization has challenged the traditional concept of definite myocardial damage in persistent, severely hypokinetic or even dyskinetic myocardial regions after myocardial infarction. The term "hibernating myocardium" has been introduced (11) to describe the chronic regional myocardial dysfunction when the severely reduced myocardial perfusion is still sufficient to maintain tissue viability at a lower level of contractility.

Therefore, it is vital to determine viability of chronically dysfunctioning myocardial regions that would benefit from the restoration of perfusion. Several methods have been attempted to detect myocardial viability based on improved regional contractile responses. These include inotropic stimulation or nitroglycerin administration as well as postextrasystolic potentiation of contraction imaged by two-dimensional echocardiography (12) and contrast or radionuclide angiography (13). Thallium-201 perfusion scans (14) as well as perfusion and metabolic studies using positron emission tomography are also considered useful techniques. However, recent investigations (15) utilizing positron emission tomography have revealed that more than half of the myocardial regions showing irreversible defects on thallium-201 images were metabolically active both in animal experiments and in human subjects imaged by F-18-fluoro-2-deoxyglucose. These studies also demonstrated that Q wave development did not provide unequivocal evidence of transmural myocardial necrosis, and furthermore did not preclude improvement in wall motion after revascularization.

Synchronized diastolic retroperfusion of the ischemic myocardium. Animal studies (6,7) have documented that synchronized diastolic coronary venous retroperfusion of the ischemic myocardium offers effective protection against severe ischemic injury. Retroperfusion improves local blood flow, including that to the most ischemic subendocardial myocardial layer, thereby improving the endocardial/epicardial flow ratio (16).

Studies (17) using digital subtraction coronary venography demonstrated that synchronized retroperfusion delivered arterial blood into the regional coronary veins of the ischemic zone. Another recent study (18) using positron

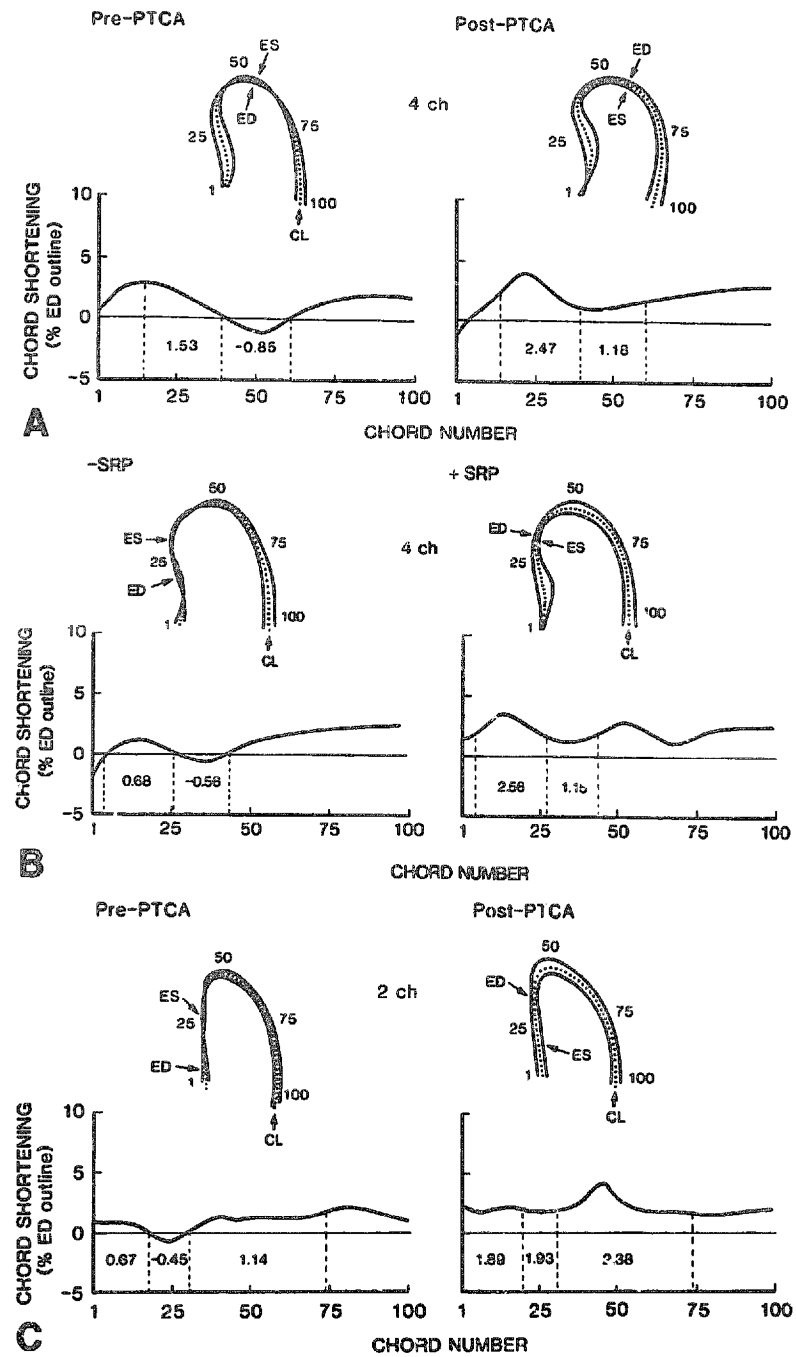

Figure 2. Graphs and left ventricular endocardial contours at end-diastole (ED) and end-systole (ES) representing two-dimensional echocardiographic regional left ventricular wall motion before, during and after percutaneous transluminal coronary angioplasty (PTCA) as quantitated by the centerline (CL) method. The given values are the average of individual chord-shortening factors in a myocardial region. Chord-shortening factors are expressed as the percent of the end-diastolic diameter. A, Chord-shortening plots and endocardial contours of apical four chamber view images recorded before (Pre-PTCA) and 30 min after (Post-PTCA) angioplasty of the left anterior descending coronary artery. Apical dyskinesia on the baseline image reverted to synergic motion and contractility of the proximal septum increased. B, Chord-shortening plots and endocardial contours of apical four chamber view images during angioplasty of the left anterior descending coronary artery performed without retroperfusion (−SRP) and with retroperfusion (+SRP). Balloon inflation without retroperfusion resulted in a further decrease in contractility of the septum, with preserved dyskinesia of the apical region. During balloon inflation with retroperfusion, contractility of the septum and apex increased to the same level as on the postangioplasty image. C, Chord-shortening plots and endocardial contours of apical two chamber view images recorded before (Pre-PTCA) and 30 min after (Post-PTCA) angioplasty. Dyskinesia of the inferior wall reverted to synergic motion, with an increase in contractility of both the posteroinferior wall and the anteroapical region.

emission tomography revealed enhanced glucose metabolism in the risk zone during simultaneous coronary occlusion and synchronized retroperfusion.

Clinical trials were recently initiated to evaluate the feasibility and safety of retroperfusion in humans in clinical settings, such as during percutaneous transluminal angioplasty (8) and in unstable angina (9). Retroperfusion proved to ameliorate ischemia by reducing chest pain and the decrease in regional and global left ventricular function.

Conclusions. In the reported case, retrograde blood supply by synchronized diastolic coronary sinus retroperfusion of arterial blood during the angioplasty procedure accurately detected areas of previously nonfunctioning but viable myocardium. One must keep in mind that retroperfusion is an invasive technique and that there are several noninvasive methods to define myocardial viability. In emergency situations or during high risk coronary interventions, synchronized diastolic coronary venous retroperfusion can effectively protect severely compromised myocardial regions from continuing ischemia as well as predict viability of chronically dysfunctioning myocardial regions that would benefit from the restoration of anterograde flow. This tech-

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nique has been proved to provide adequate arterial blood supply retrogradely in the region of the left anterior descending coronary artery. Studies have been undertaken to investigate the possible benefit of retrograde blood supply in the left circumflex and right coronary artery territories as well.

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